

## EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S1	0	("fusedimidazole").PN.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2006/05/05 17:21
S2	398088	fused imidazole	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/05/09 14:18
S3	515170	fused imidazole and neurodegenerative disorder	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/05/05 17:23
S4	514976	fused imidazole with neurodegenerative disorder	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/05/05 17:23
S5	1437	(fused imidazole) with (neurodegenerative disorder)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/05/10 12:11
S6	2	"6855711"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/05/05 18:12
S7	2	"6531464"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/05/05 18:17
S8	2	"6175015"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/05/05 18:19
S9	5	"6133299"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/05/05 18:19

## EAST Search History

S10	2	"6737424"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/05/05 18:45
S11	384	"fused imidazole"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/05/09 15:33
S12	19	"fused imidazole" and "neurodegenerative disorders"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/05/09 14:54
S13	19	("fused imidazole") and ("neurodegenerative disorders")	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/05/09 14:55
S14	3	"20030130289"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/05/09 15:41
S15	3	"6900214"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/05/09 15:44
S16	6	"6900218"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/05/09 15:45
S17	2	"6960685"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/05/09 15:48
S18	2	"6417189"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/05/09 15:51
S19	5	"6696039"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/05/10 09:43

## EAST Search History

S20	4	"6696039"	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 16:41
S21	2525560	neurodegenerative disorder increased neurons	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 16:42
S22	2525560	neurodegenerative disorder increased neurons	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 16:42
S23	216	(neurodegenerative disorder increased neurons)and (S11)	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 18:14
S24	173	(neurodegenerative disorder "increased neurons")and (S11)	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 18:11
S25	1	(neurodegenerative disorder "increased neurons")and (S11)and (neurogenesis)	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 18:12
S26	1	(neurodegenerative disorder "increased neurons")and (S11)and neurogenesis	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 18:12
S27	1	(neurodegenerative disorder increased neurons)and (S11)and neurogenesis	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 18:12
S28	2519076	neurodegenerative disorder increased neurons and (S11)and neurogenesis	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 18:13
S29	1	(neurodegenerative disorder increased neurons) and (S11)and neurogenesis	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 18:13
S30	0	neurodegenerative disorder increased neurons and (S11)and neurogenesis	US-PGPUB; USPAT; USOCR; EPO; JPO	AND	ON	2006/05/09 18:13
S31	0	neurodegenerative disorder increased neurons and (S11)and neurogenesis	US-PGPUB; USPAT; USOCR; EPO; JPO	WITH	ON	2006/05/09 18:13

## EAST Search History

S32	1	(neurodegenerative disorder increased neurons)and (S11)and neurogenesis	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 18:14
S33	31	(neurodegenerative disorder increased neurons)and (S11)and neurons	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 18:53
S34	2	"9839343"	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 18:56
S35	4	"6518273"	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 18:59
S36	14	"5334606"	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 19:00
S37	38658	fuzed imidazole with increase neurons	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 19:00
S38	484	(fuzed imidazole) with (increase neurons)	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 19:40
S39	6988	(fused imidazole) with (increase neurons)	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 19:03
S40	7	(fused imidazole) with (neurogenesis)	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 19:01
S41	184417	(fused imidazole)and (increase neurons)	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 19:02
S42	7	"6048896"	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 19:04
S43	89	"6239288"	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 19:35

## EAST Search History

S44	103205	neuron growth and fused imadzole	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 19:36
S45	80155	(neuron growth) and fused imadzole	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 19:36
S46	80153	(neuron growth) and (fused imadzole)	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 19:36
S47	3868	(neuron growth) with (fused imadzole)	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 19:36
S48	32	("neuron growth") with (fused imadzole)	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 19:37
S49	0	("neuron growth") with ("fused imidazole")	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 19:37
S50	0	("neuron growth") and ("fused imidazole")	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 19:38
S51	253	("neuron growth") and (fused imidazole)	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 19:39
S52	0	("neuron growth") and (fused imidazole)and neurodegenerative	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 19:39
S53	0	("neuron growth") and (fused imidazole)and (neurodegenerative)	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 19:40
S54	523	(fused imidazole) with (increase neurons alzheimers)	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 20:24
S55	0	"200162704"	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 20:25

## EAST Search History

S56	3	"0162704"	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 20:25
S57	1	"2000162704"	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 20:25
S58	2	"00162704"	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2006/05/09 20:25
S59	2	"20020107273"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/05/10 10:28
S60	8	"6284539"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/05/10 10:28
S61	3	"9936415"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/05/10 12:25
S62	2	"6699871"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/05/10 12:25

[advan](#)
[Home](#)[About Us](#)[Browse](#)[Search](#)[My Liebert](#)[Help](#)[Cor](#)[Welcome, Us Patent & Trademark Office](#)[Sign](#)

## Journal of Clinical Laser Medicine & Surgery

### Modulator of Heme Biosynthesis Induces Apoptosis in Leukemia Cells

Apr 2001, Vol. 19, No. 2: 59-67

Natalie Rebeiz, PhD, Sean Arkins, PhD, K.W. Kelley, PhD, Gary Durack, MS,  
Constantin A. Rebeiz, PhD

**Objective:** The purpose of this research is the investigation of the possible cause(s) of the dark-cell death phenomenon induced by 1,10-phenanthroline (Oph), a porphyrin biosynthesis modulator. **Summary Background Data:** We have previously shown that porphyrin biosynthesis modulators, such as Oph, which is also an ironchelating agent, enhance protoporphyrin IX (Proto) accumulation in mammalian neoplastic cells treated with  $\delta$ -aminolevulinic acid (ALA). As a result of the enhanced Proto accumulation, a significant increase in photo-dynamic damage was observed under illumination. Also tetrapyrrole and heme-biosynthesis modulators have been shown to cause death in treated insect larvae in darkness, a phenomenon referred to as dark-cell death. Dark-cell death was also observed in Oph + ALA-treated transformed mammalian cells. **Methods:** Neoplastic cells were treated with ALA, Oph, and ALA + Oph, and the following cell properties were investigated: growth arrest, membrane permeability, cell survival, nucleosomal cleavage, and cell cycle alterations. **Results:** It was observed that Oph but not ALA induced growth arrest, in a T-cell leukemia line (MLA 144) as assessed by reduction in DNA synthesis. Exogenous Proto and isomers of Oph lacking the iron-chelating property of Oph also caused a dose-dependent inhibition of proliferation in MLA 144 cells. Although the plasma membrane of Oph-treated cells remained intact following 3 h of dark-incubation, the cells exhibited DNA internucleosomal cleavage, characteristic of cells undergoing apoptosis. Cell cycle analysis using the DNA intercalating dye propidium iodide (PI) coupled to flow cytometry, indicated that  $81 \pm 5.6\%$  of Oph-treated MLA 144 cells were apoptotic, with the majority of the cells arrested in the early S phase. On the other hand, treatment with either ALA or Proto did not alter the cell cycle. Also, using a double-labeling protocol with Hoechst 33342, and PI, and analysis by flow cytometry, Oph-treated cells were found to be 82% apoptotic after 3 h of dark-incubation. Apoptosis was reduced by 75% ( $p < 0.05$ ) by the cytoplasmic protein synthesis inhibitor cycloheximide. **Conclusions:** These results indicate that in addition to enhancing Proto accumulation, the heme biosynthesis modulator Oph also induces growth arrest and apoptosis in transformed cells in darkness.

[All Papers](#)[← previous](#)**Full Text PDF:**

- [For printing](#)
- [With links](#)
- [Help with PDFs](#)

- [Add to favorites](#)
- [E-mail to a colleague](#)
- [Track citations](#)
- [Download metadata](#)

- [PubMed citation](#)
- [Related papers in Liebert Online](#), [PubMed](#)
- [Most read paper](#)

**Search:** [Liebert Online](#) **Authors:**

- ☐ Natalie Rebeiz  
☐ Sean Arkins  
☐ K.W. Kelley  
☐ Gary Durack  
☐ Constantin A. Rebeiz

**Keyword:**


  
[Advanced](#)

### This paper was cited by:

#### Histone hypoacetylation is involved in 1,10-phenanthroline-Cu<sup>2+</sup>-induced human hepatoma cell apoptosis

Jiuhong Kang, Jie Chen, Yufeng Shi, Jie Jia, Zhenhua Wang

JBIC Journal of Biological Inorganic Chemistry. 2005, Vol. 10, No. 2: 190

[CrossRef](#)

#### Necrotic cell death induced by delta-aminolevulinic acid in mouse astrocytes. Protective role of melatonin and other antioxidants